Space Biotech: Hindsight, Insight, Foresight

Presentation to:!
!

EXOMEDICINE! WORKSHOP!

!
sponsored by!
KentuckySpace!
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20 May 2015!
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"

NASA Ames Research Center"
Lynn Harper, Lead Integrative Studies"
Space Portal"
Level 2 Emerging Space Office"
Partnerships Directorate"

Space Biotech

Hindsight, Insight, Foresight

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"

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FASEB"

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"


BEYOND
the PLANET
of ORIGIN

Prevent Death"

All Intensive Care Wards Worldwide are based on Apollo Medical Telemetry

Enable Life™

Spinoff: Fetal Biotelemetry System"

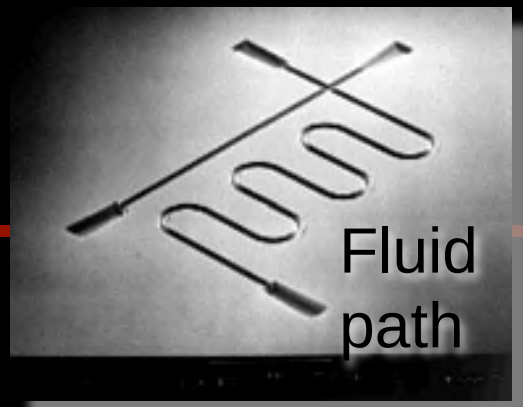
- *Fetal Health Status Monitor*
- *pH/temp/HR Fetal Biotelemetry System*
- *pH/temp/ECG/pressure Fetal Biotelemetry System*

Collaborative development efforts with UCSF Fetal Treatment Center

NASA Ames Exploration Probes and Small Satellites Group

Generate Wealth™

reactor



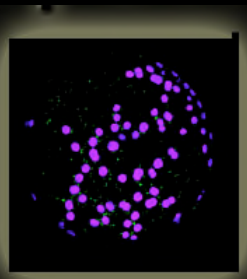
pump

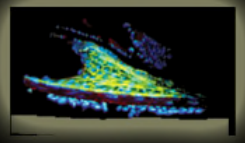
Biotech-Infotech-Superminiaturization revolutions amplify the *value* of a payload pound to space a million times or more over what was possible 5 years ago. Space Bio MEMS advances generate $2B+ annually

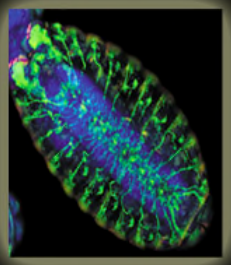
motor

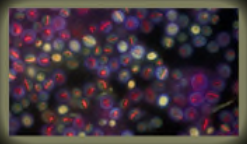
What's New Since the Last Time We Went to the Moon?"

Technology Revolutions"









PARADIGM BUSTERS!"

"

Biotech revolution"

"

Infotech revolution"

"

MEMS /nanotechnology"

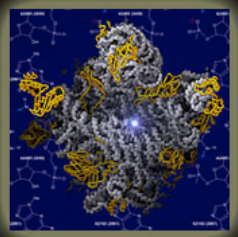
Opens **previously inaccessible biological regions"**

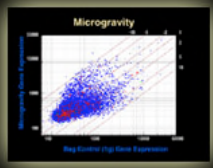
"

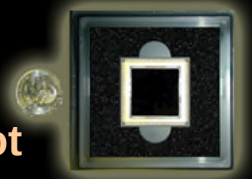
Amplifies **the value of a biosciences payload pound by orders of magnitude"**

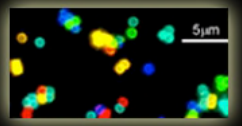
"

Reveals **features of terrestrial life that cannot be seen on Earth"**









The biotech revolution provided the equivalent of a Hubble Space Telescope for Space Biosciences"

Astronomy biology parallels"

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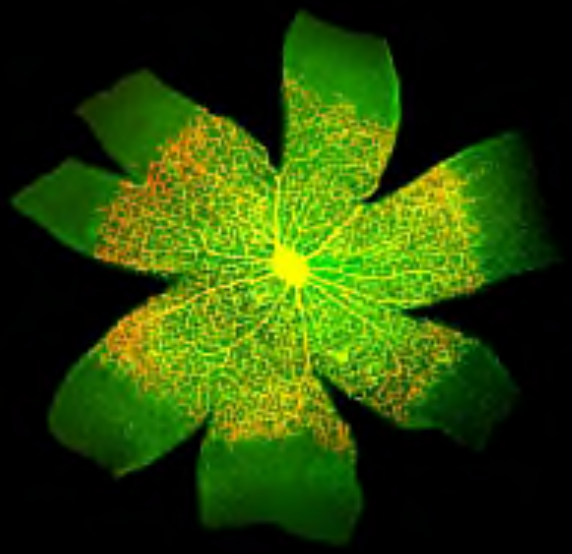
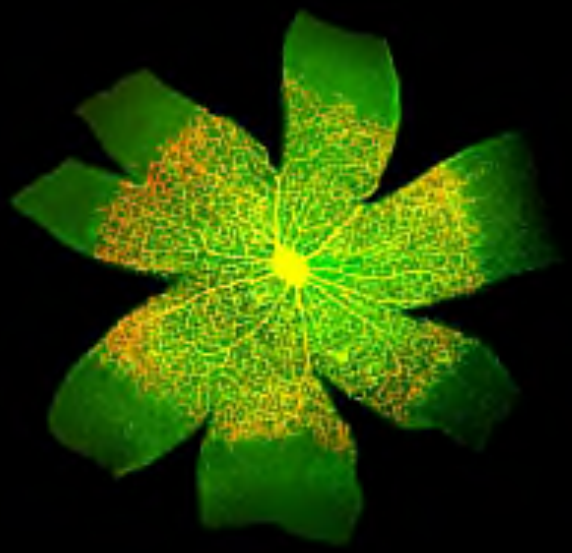
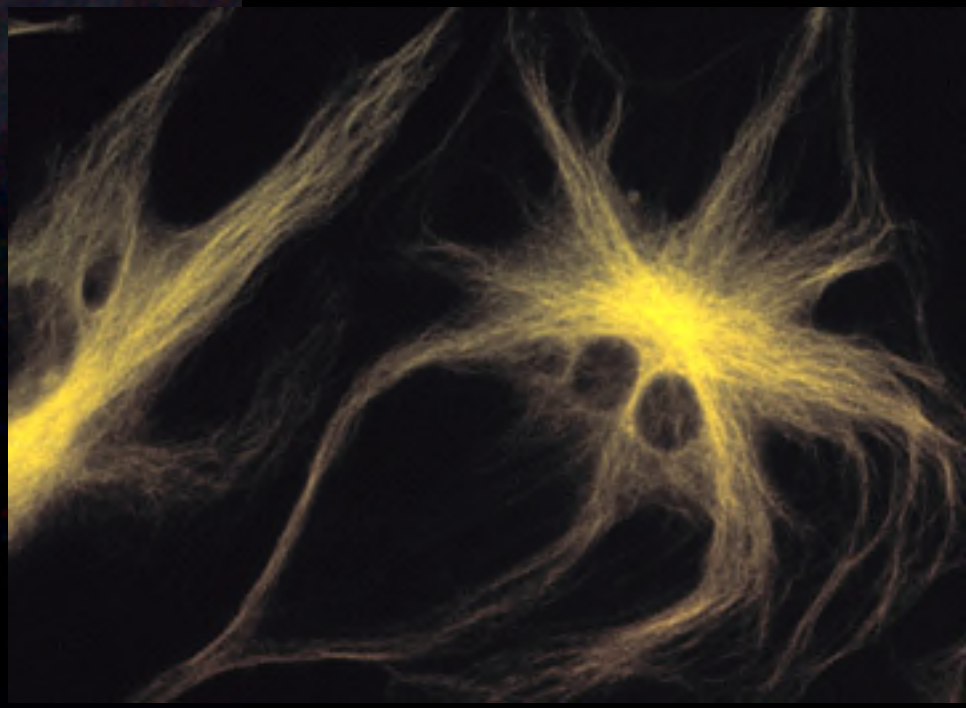


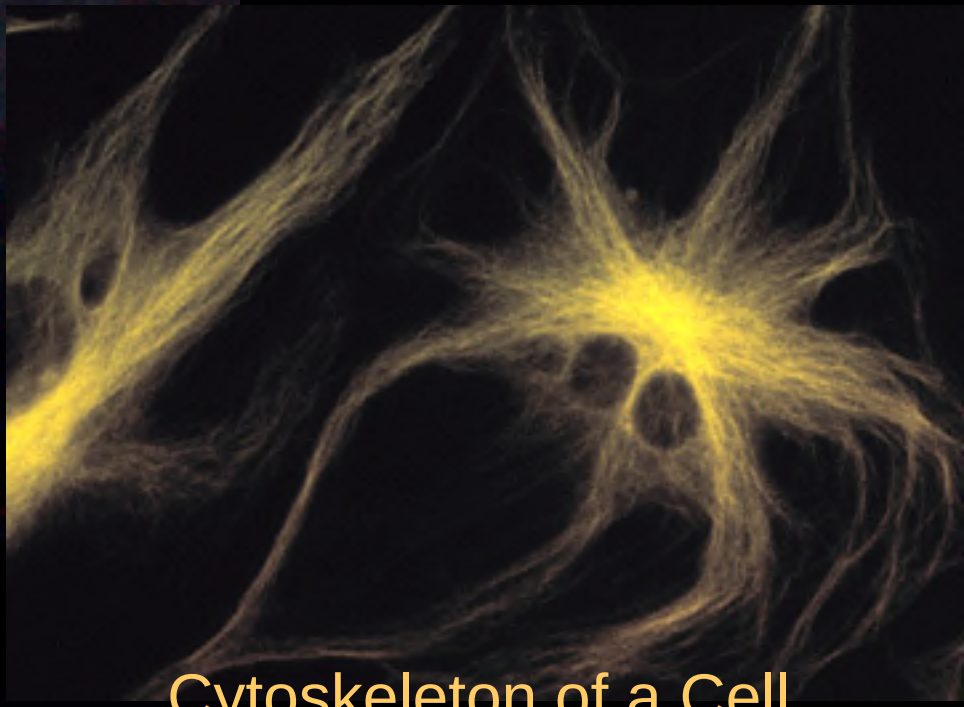
Retina of a Mouse's Eye



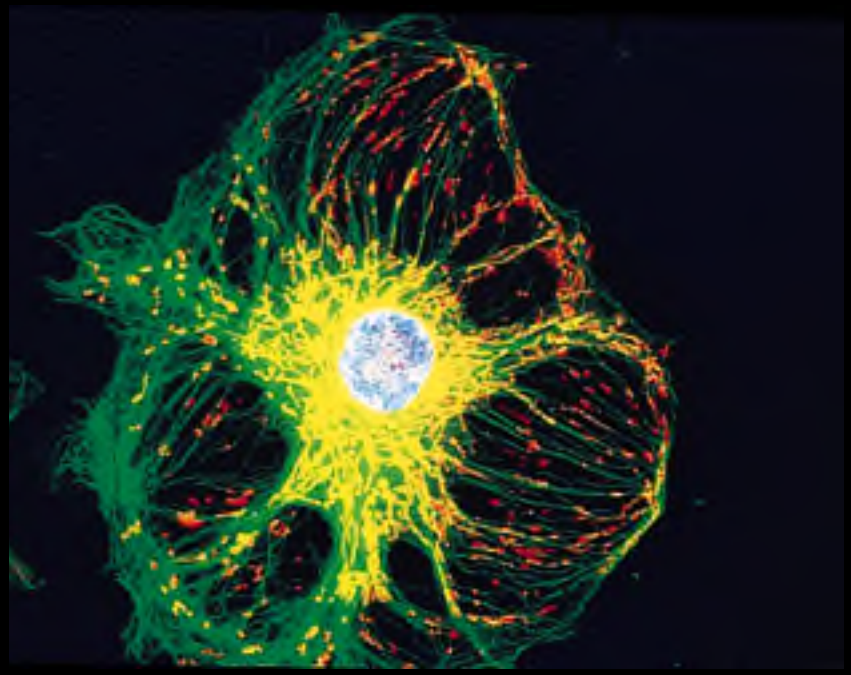
Star Exploding



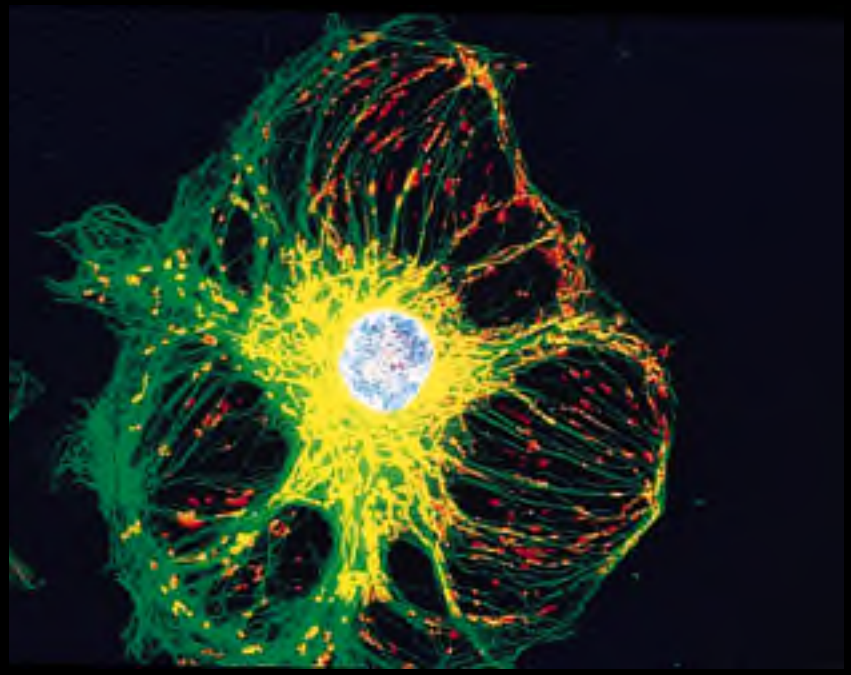
Molecular Cloud in Space
Light years distant, light years in size



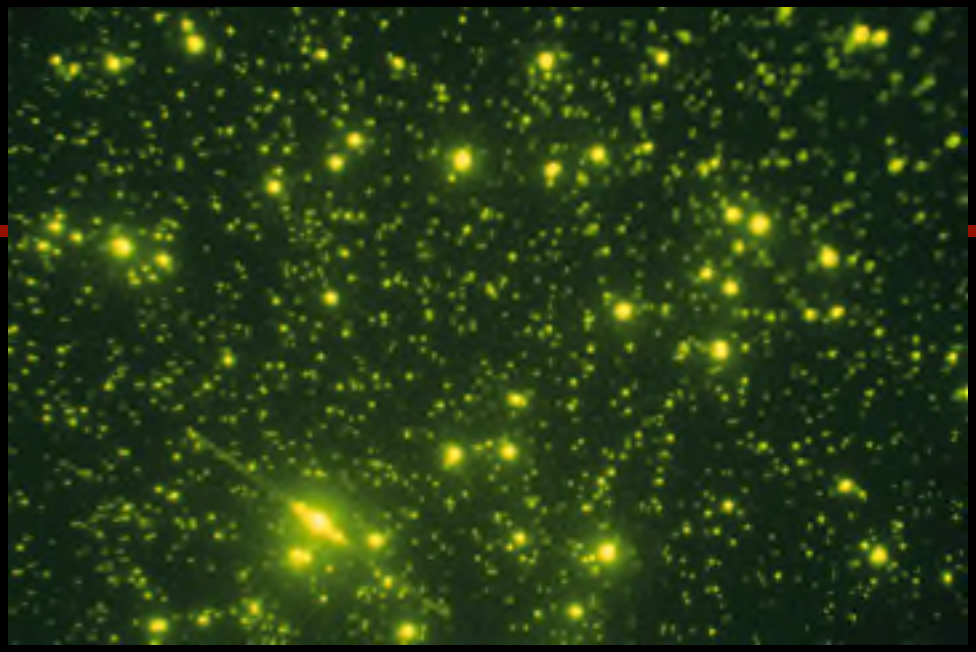
Cytoskeleton of a Cell
Less than 100 microns

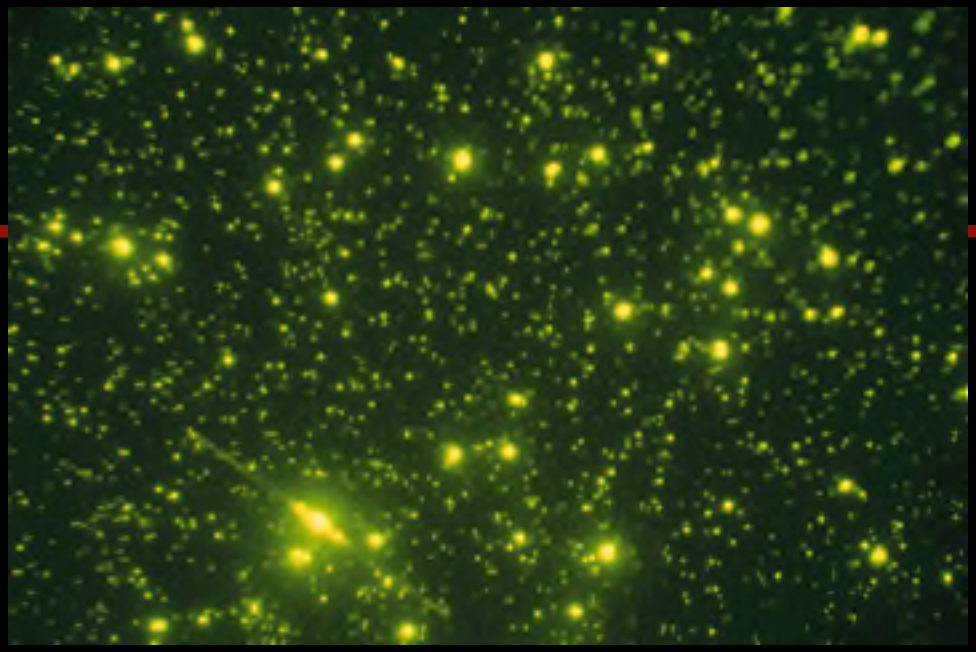


Nucleus, mitochondria, cytoskeleton
Of a cell less than 100 microns



Birthplace of more than 700 stars
Light years from Earth
Light years in size





A drop of seawater
With only the DNA illuminated
Small “stars” are viruses
Medium “stars” are bacteria
Galactic looking object is a diatom

Hubble Space
Telescope
Deepfield Study
12 billion light years

Investigations"

- # Emerging Space Office (ESO) Commercial Microgravity Case Studies 2012-present"
  - # Identify high value areas where gravity is limiting American industry and determine whether and how the ISS or other U.S. commercial LEO platforms can enable necessary breakthroughs."
  - # Identify where gravity is hindering medical research and applications and determine whether and how the ISS or other U.S. commercial LEO platform can contribute to important advances."
- # Space Commercial Laboratory Applications Working Group 2010-2011"
- # ISS National Laboratory Workshop chaired by Nobel Laureate Blumberg October 2007 with keynote address by Dr. J. Craig Venter identified strategies for implementing the ISS as first National Lab beyond Earth that lay the content for the Oct workshop."
- # Commercial Space Forum (May 2006) identified specific development projects and teams. "

Background

- Emerging Space Office (ESO), reporting to the NASA HQ Chief Technologist, was established in 2012 to provide economic intelligence on the rapidly developing space ecosystem."
- One of the first studies was to examine the potential of microgravity to affect the nation's economy and general welfare."
- Focus was on terrestrial markets rather than NASA applications, applied rather than basic research, and commercial rather than academic investigators. "
- The ISS was the centerpiece of these studies, but commercial microgravity also affects emerging commercial laboratories such as SpaceX DragonLab, Bigelow Aerospace expandable modules, and suborbital spacecraft and third tier suppliers like CASIS, Nanoracks, Bioserve, TechShot, etc."

"Extraordinary claims require extraordinary evidence."

– Carl Sagan

Note: The candidate technologies contained in this document do not yet have sufficient evidence to confirm their value as marketable products from microgravity manufacturing. That is, in fact, the point of the proposed flight activities. In all cases, we have obtained, or are in the process of obtaining independent validation of pre-ISS flight claims and also recommend independent validation of ISS flight results.

Findings"

Many of the problems that hindered space research and space commercial development either have been solved or are close to being solved:"

- **Technology is ready and often on the shelf to enable discovery and development in space."**
- **Wealthy individuals self-financing their own rockets and space stations."**
- **Flight frequency has increased because of commercial providers"**
- **Diverse customer base that wants to fly."**
- **Private capital looking towards space for investment opportunities."**
- **New customers close or at the point of closing the business case for space products."**
- **New space markets identified."**
- **Humanitarian space projects identified."**

Low-Hanging Fruit"

- Three case studies for commercial development from microgravity are presented as examples for understanding different features of commercial needs/opportunities in the near future. (There are 10+ additional areas under investigation.)"
  - **Silicon Carbide Wafers"**
  - **Exotic Glasses and Fibers"**
  - **3-D Tissue Engineering"**

"

- Case Studies:"
  - Meet the criteria of a general-purpose technology as defined by NRC"
  - Offer high probability of significant potential impact of the product on the nation (multiple billions of dollars or health benefits affecting millions of people)"
  - Product clearly requires microgravity for development or improvement"
  - Companies are actively seeking solutions in microgravity because of 1-g limitations"
  - Prior microgravity research strongly indicates that the desired product outcome could be achieved in space"
  - Flight hardware exists now or can be easily modified to enable on-orbit investigations/manufacturing"

"

"

Opportunities: Doing Good While Doing Well"

- #Reveal the biological story of the only life that we know during its first generations beyond the planet of origin."
- #Use the results to enable better futures for humanity."
- #Generate wealth and promote the new space economy."

Astronaut Don Pettit
Space Station Expedition Six
Speaking at the ISS National Lab Workshop

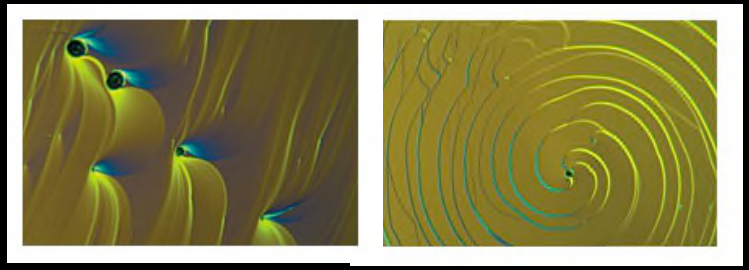
“this is why we go to a frontier ! to go
where our intuition no longer applies.”

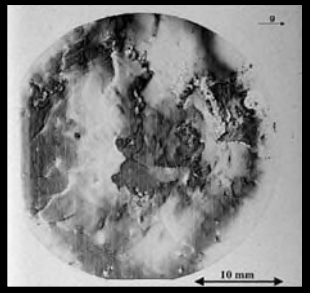
Silicon Carbide (SiC) Wafers Summary"

Value of Microgravity Manufactured Product: Very High"

- SiC operates at 1000°C versus 300°C for silicon based devices, withstands 10X electric fields over silicon, offers high radiation resistance, high thermal conductivity, high maximum current density and more"
- Immediate market. SiC could replace silicon in hybrid and electric cars, enable much faster and much more energy efficient computers, provide new sensors for extreme environments, and other unique applications"
- Opens new classes of products and microgravity research (e.g. GaN semiconductors)"
- Component sales estimated well in excess of $10B/ year and growing"
- Multiple consumer military, energy, NASA applications with values many times greater than the wafer sales."

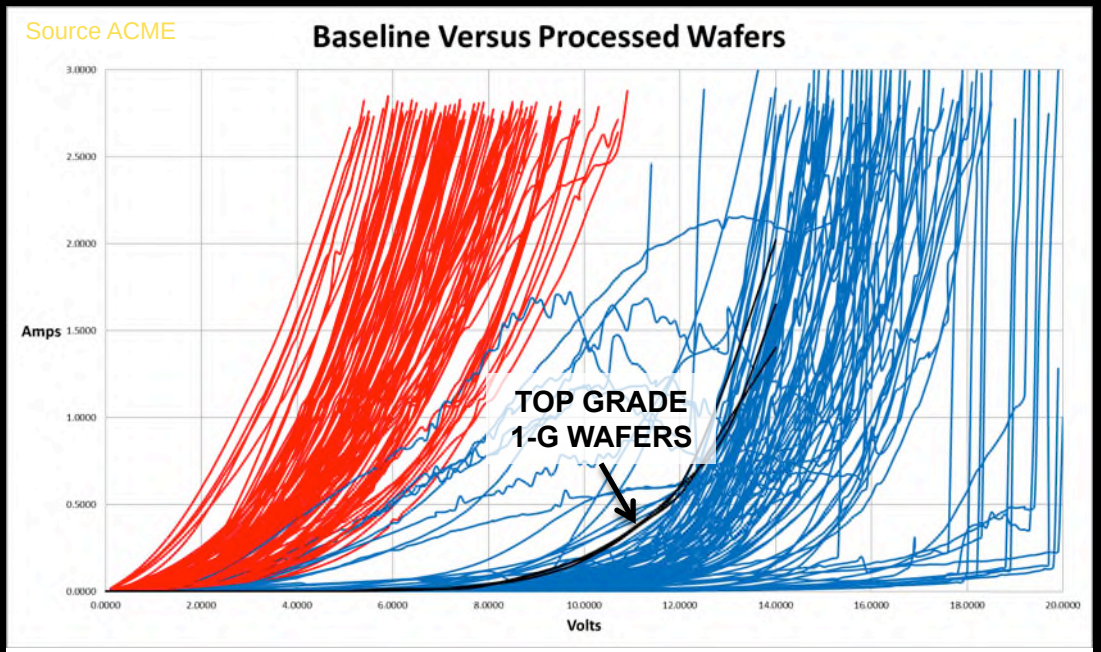
Gravity causes high defects in silicon carbide crystal growth on Earth limiting size of wafers, increasing manufacturing cost, and restricting applications."





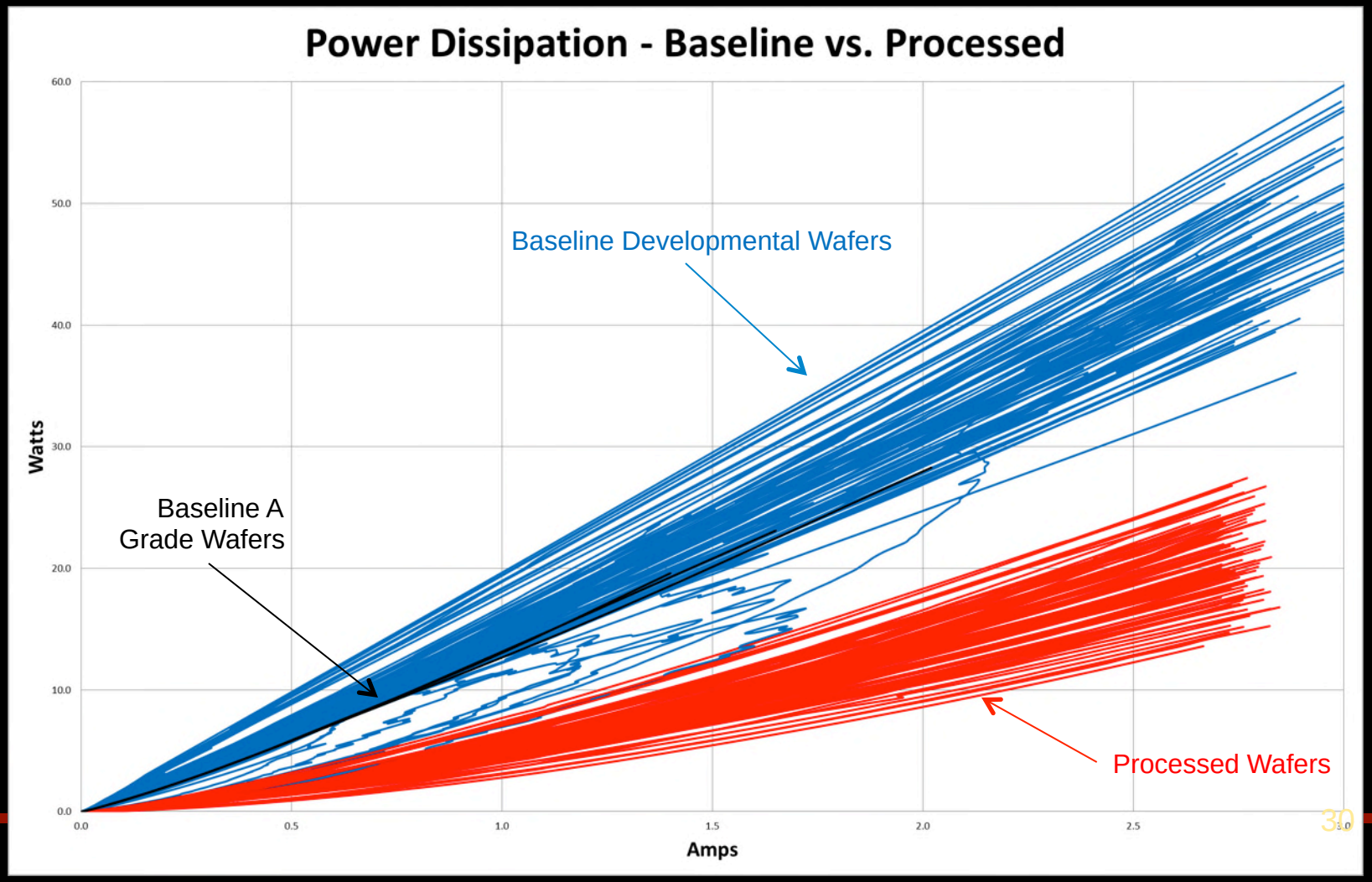
Silicon Carbide (SiC) Wafers Summary"

- Readiness: Manufacturing already proved in space (TRL 7)"
  - ACME Advanced Materials Inc has flown 100 “junk” 4 inch SiC wafers (sold at $250/wafer), “healed” them in space with reported 99% success, which resulted in wafers better the best manufactured on Earth (sold at $1500/wafer and shown as the black line in the graph below). "
  - 100+ wafers can be processed in minutes in space."
  - Microgravity significantly improves crystal lattice structure resulting in much lower defects"
  - ACME claims 82% gross margin"

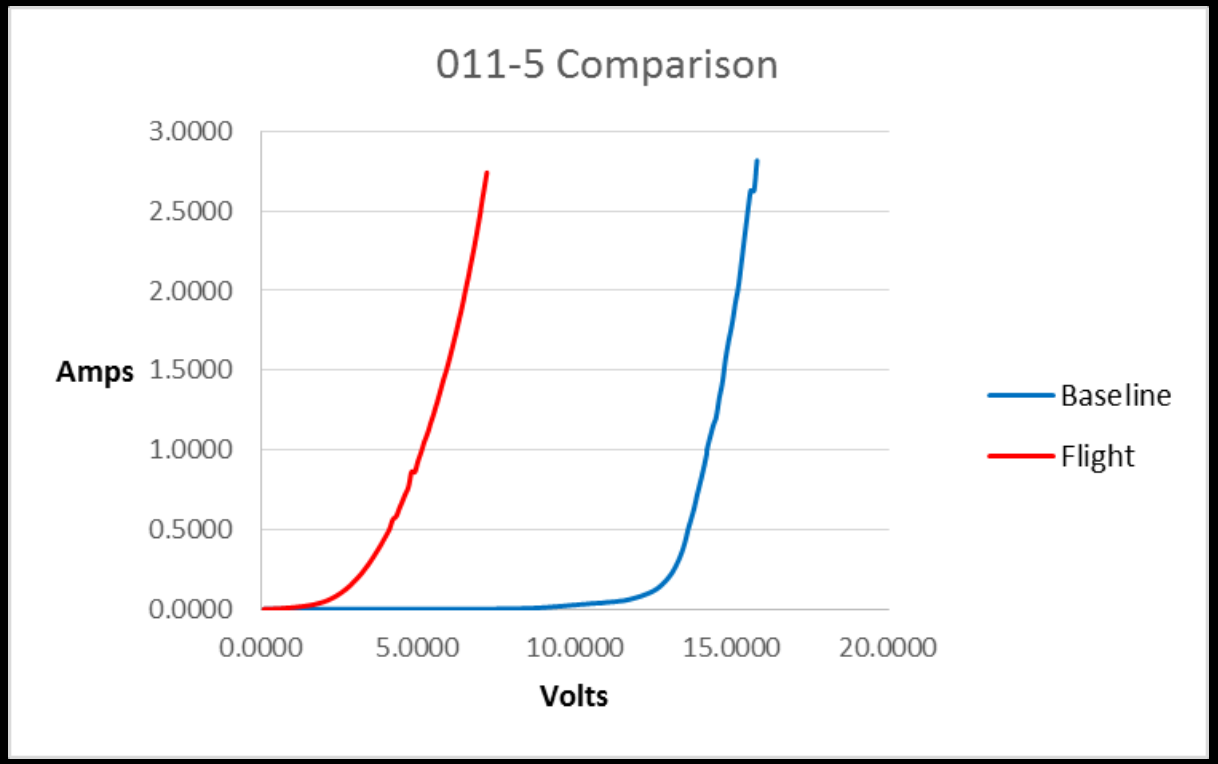


Red = after flight processing. Blue = before flight processing. Black = Top grade 1-g
This graph shows the IV response for 100 development grade 4” SiC wafers (II-VI, Corning, and C grade Chinese). Current through the wafer – not lateral. Note the wide variation in response of the unprocessed wafers versus the processed wafers.

in the processed wafers when compared to the unprocessed wafers



SiC Before and After!
µg Processing!
"



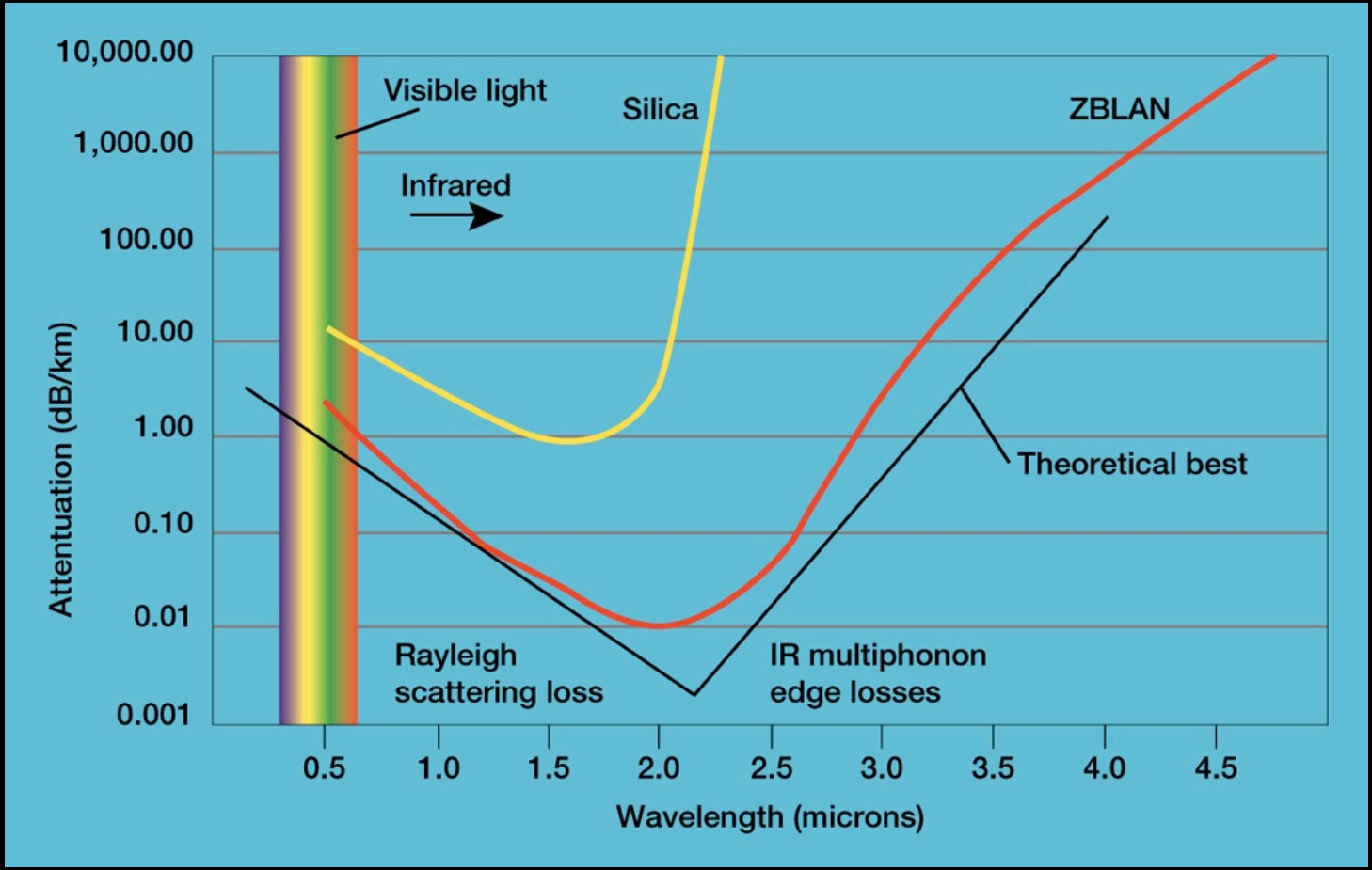
Exotic Glasses and Optical Fibers Summary"

- Value of Microgravity Manufactured Product: Potentially Very High"
  - Enables unique growing medical, military, sensor, consumer, and communications products estimated > $10B/yr"
  - Immediate market for some applications, other markets depend on availability of higher quality products. "
  - Exotic fibers, e.g. ZBLAN, could replace silicon fiber optics as the backbone of the global communications market"
  - Even with reasonable launch costs, business cases could close"
  - Multiple consumer military, energy, NASA applications with values many times greater than the glass or fiber sales."
- Exotic glasses are made by melting together dissimilar and often immiscible materials Gravity causes high defects because of density differences and convection, which constrains length of fibers that can be produced."

"

ZBLAN Component	Density	Formula

Exotic Glasses and Optical Fibers"



Exotic Glasses and Optical Fibers"

- Readiness: Parabolic flights showed significant improvement in producing ZBLAN preforms and fibers (TRL 5) but needs kilometer lengths of superior quality fibers to open new markets"
  - Flight hardware proven on parabolic flights would have to be modified for ISS"
  - Iteration needed before practical manufacturability achieved. In theory, in a ~50kg flight manufacturing unit, 1 kg of exotic glass preform can produce 3-7 kg of fiber in under 30 minutes. Potential sales value ranges from $450K/kg-preform to $21,000K/kg-preform depending on composition and quality."
- ISS could enable demonstrations of the value of microgravity for a wide range of exotic glasses and fibers, provide R&D environment to perfect µ-g manufacturing, and open new market opportunities."

3-D Engineered Tissues Summary"

- # Value of Microgravity Manufactured Product: Potentially Very High"
  - # Potentially enables cancer diagnoses and treatments (Vivo Biosciences Case Study), also development of a wide range of new medical treatments"
  - # Immediate market for some applications, other markets depend on availability of higher quality products. "
  - # Meeting significant need for higher quality tissue cultures is hampered by gravity"

"

- # Space Shuttle and ISS showed improvements in size and quality of 3-D Tissues in space however this high value area still needs considerable investment and development (TRL 3)"
  - # Managing 3-D tissues in microgravity must be developed such that the tissues exhibit little or no variability from spaceflight"
  - # Flight hardware is available and some on ISS to make progress"

- # ISS could enable development of this medically important field, but it will take funding and likely consortia conducting iterative research in space."

- # Status: Independent validation completed of Vivo Biosciences study by Nobel Laureate Baruch Blumberg, Dr. Todd Meyyerose/Whitehead Institute. No path to flight yet."

"

1982 – 2000

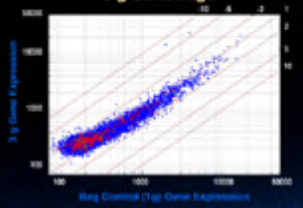
Gravity and Biology

Changes in Gravity

Renal Cells

Microvilli

3 g Centrifuge



RWV 1G

3G

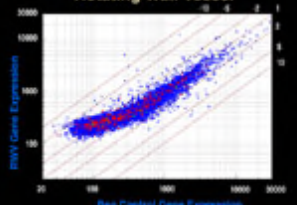
Hammond, T.G., F.C. Lewis, T.J. Goodwin, et. al. Gene expression in space. Nature Medicine 5:359 1999

Gravity and Biology

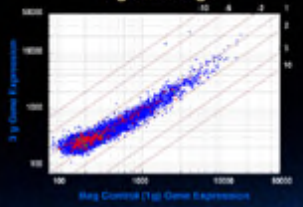
Changes in Gravity

Renal Cells

Rotating Wall Vessel



3 g Centrifuge



Microvilli

MIR

RWV 1G

3G

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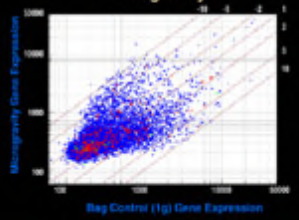
Gravity and Biology

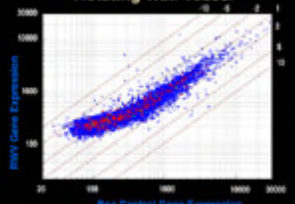
Changes in Gravity

Renal Cells

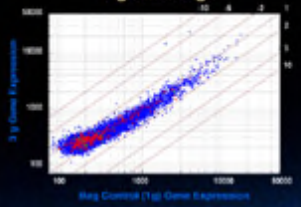
Microgravity



Rotating Wall Vessel



3 g Centrifuge



Microvilli

MIR

RWV 1G

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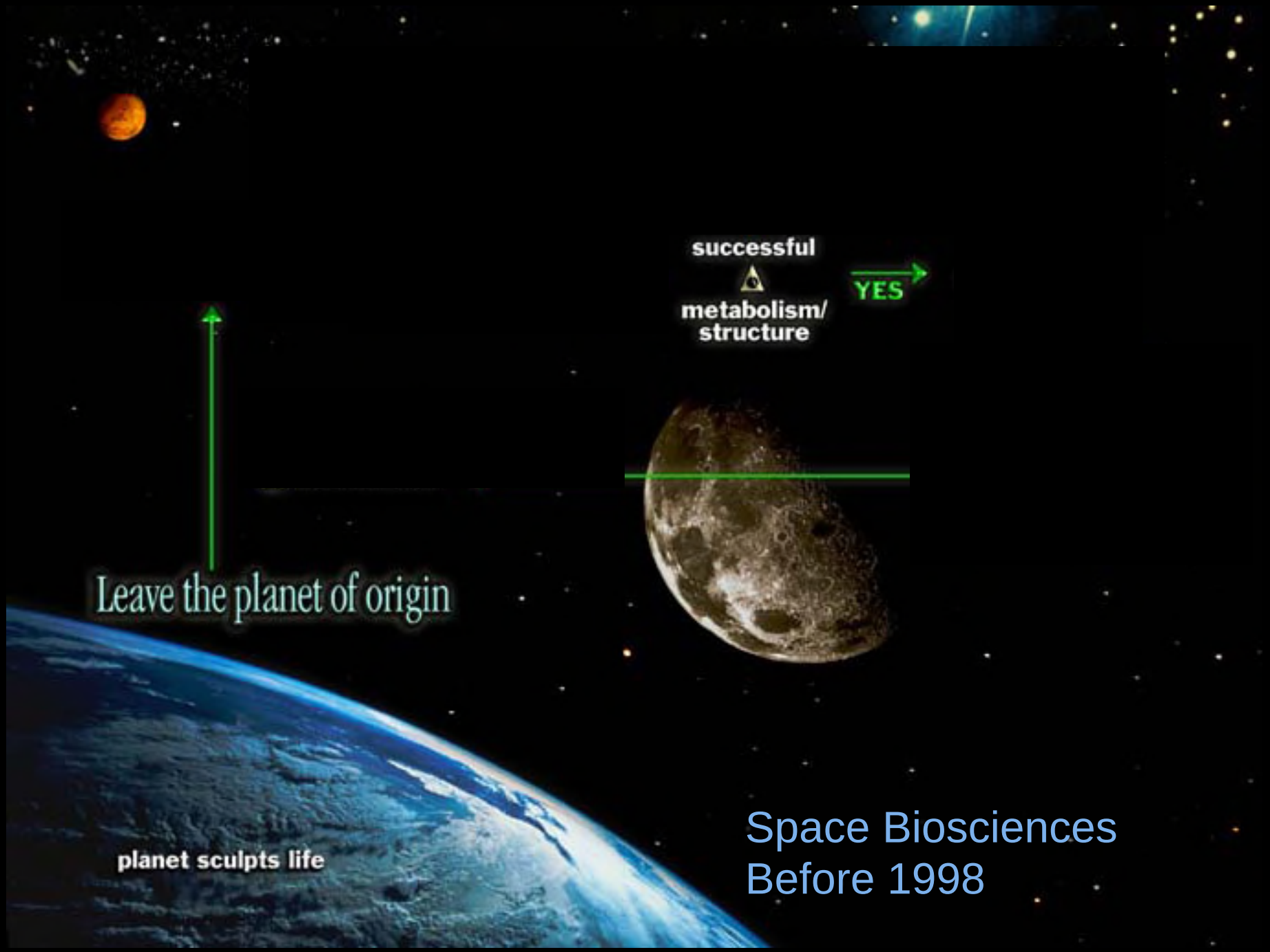
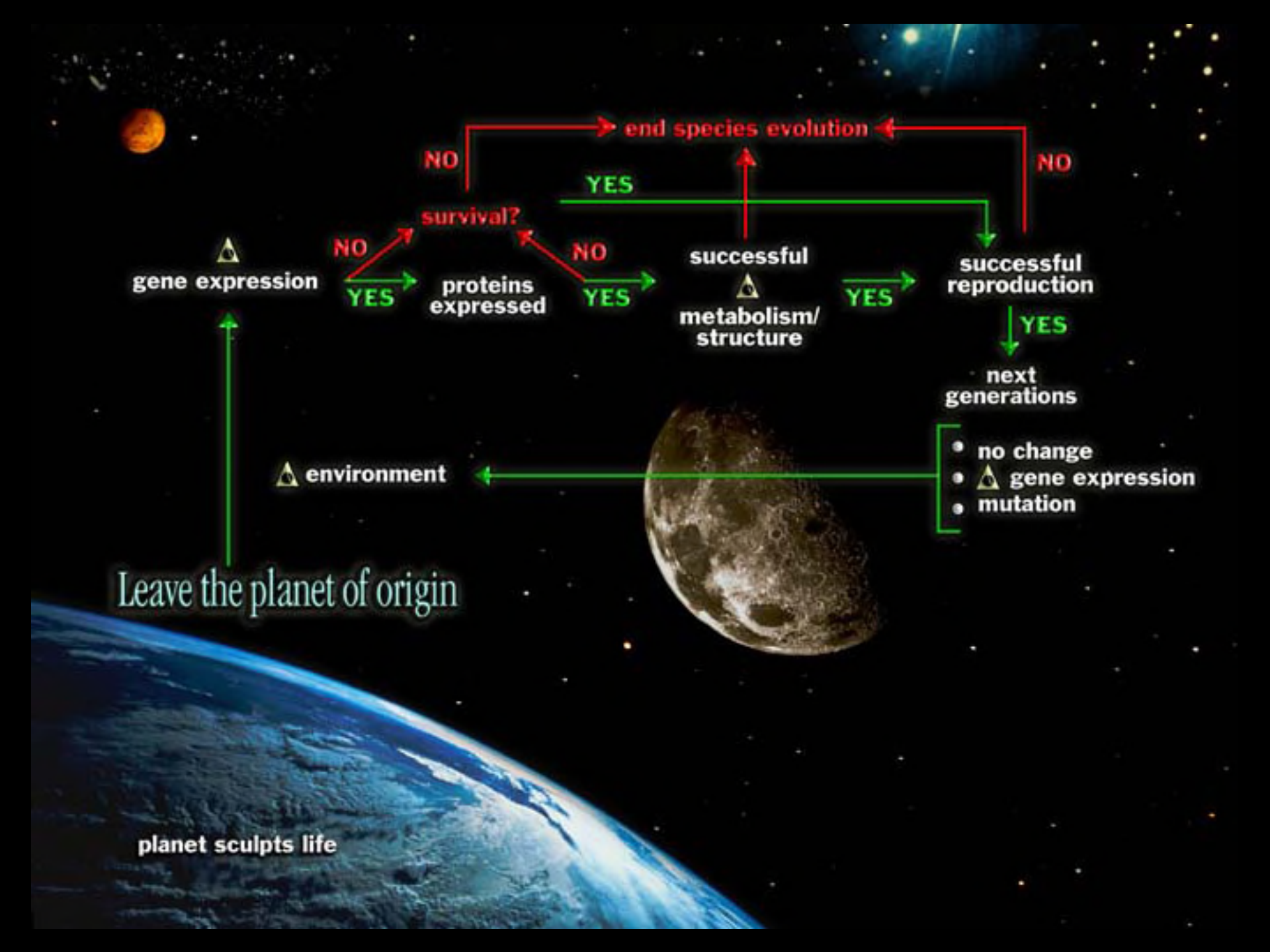
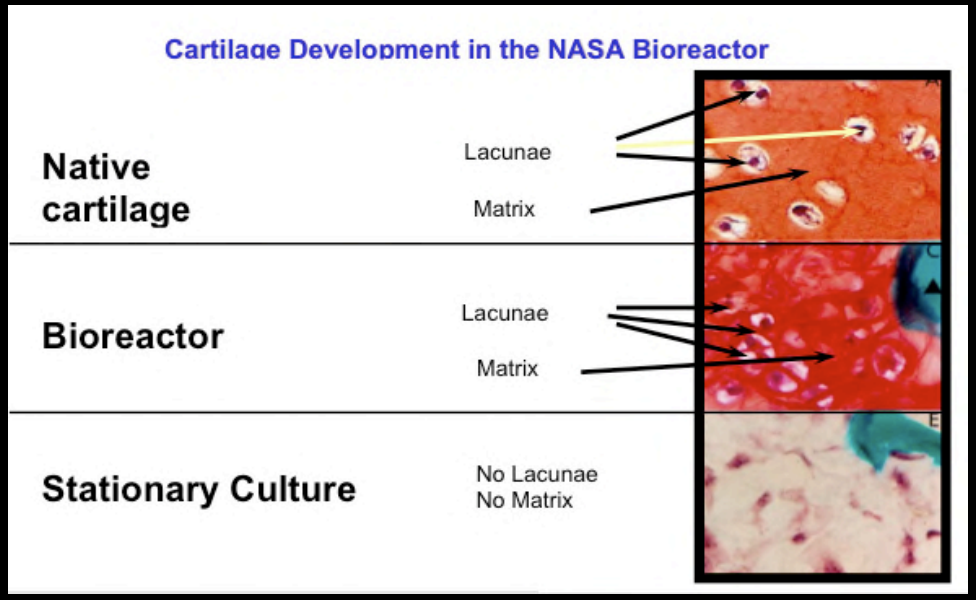


Space Biosciences
Before 1998

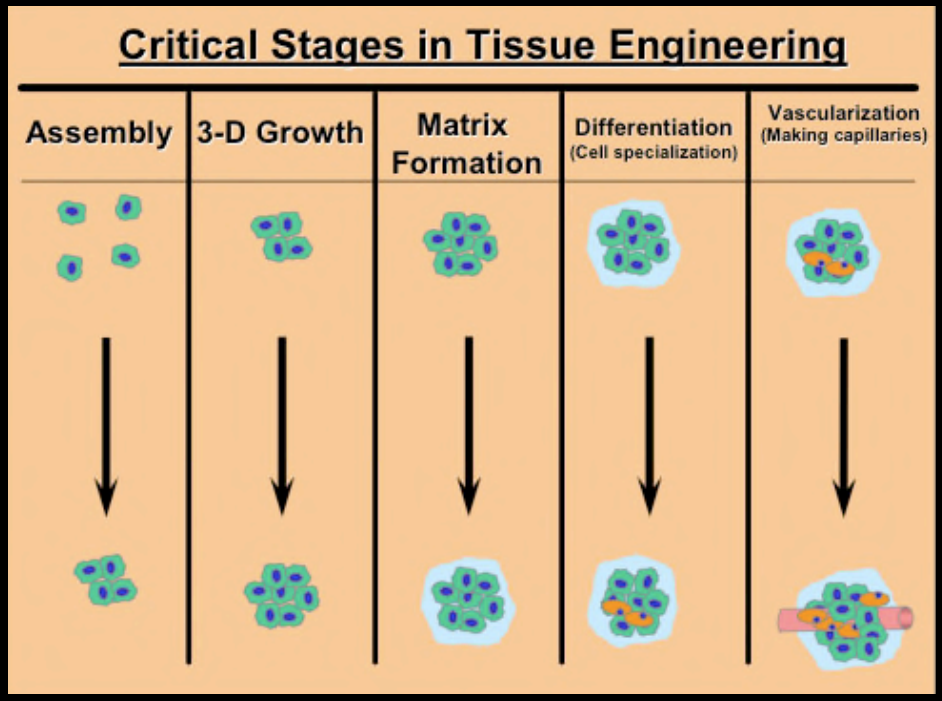

end species evolution
NO
NO
YES
survival?
NO
NO
gene expression
YES
proteins expressed
YES
successful
metabolism/ structure
YES
successful reproduction
YES
next generations
no change
gene expression
mutation
environment
Leave the planet of origin
planet sculpts life

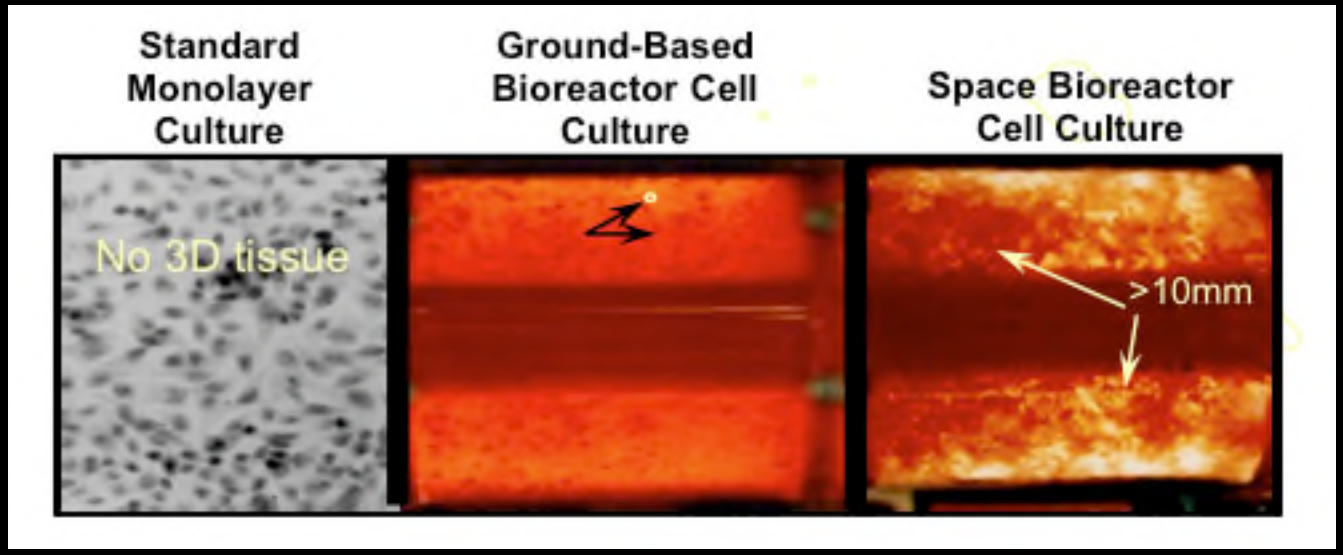
Why Space for Biotech?"

- # Good cell/tissue cultures reduce the time to the discovery of the cause of a disease and evaluation of potential cures by years to decades saving millions to billions of dollars and lives."
- # The value of a cell/tissue culture depends entirely on how well the culture mimics what happens in the body."
- # The cells are not smart but they are adaptable. Give them the wrong environmental information and they will respond biologically in medically misleading ways. "
- # The size and complexity of a tissue culture is limited on Earth by gravity."
- # Similarly high quality protein crystals accelerate drug discovery. The size and quality of some of the world's most medically important proteins is limited by gravitationally driven convection forces."

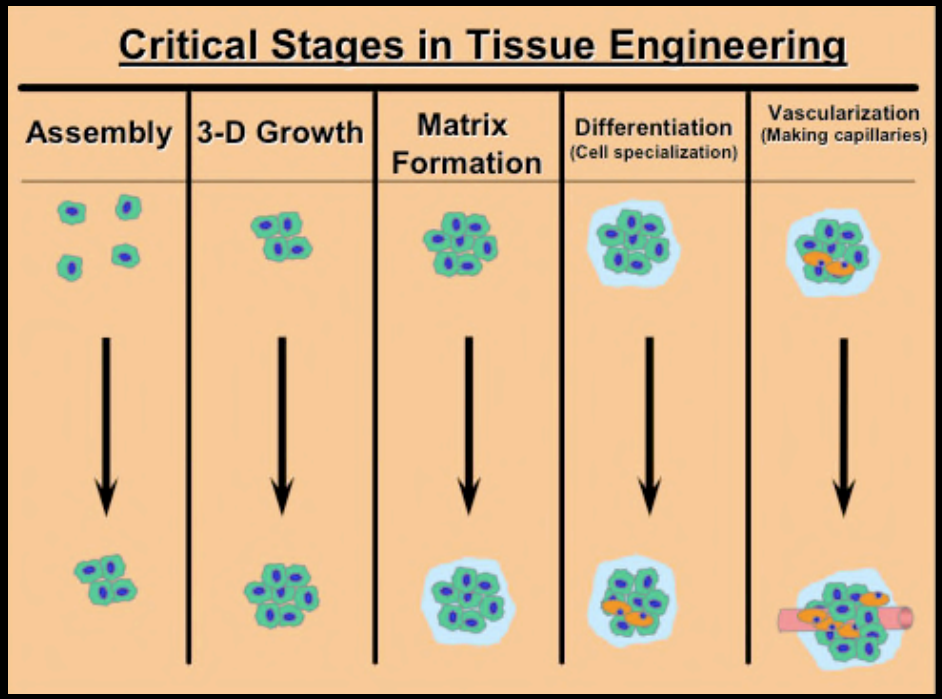


Cartilage - relevance: Osteoporosis





Colon Cancer -
Superior assembly
Beginning of differentiation



Why grow crystals in space?

The limiting step in solving complex three-dimensional protein structures needed for drug discovery is often the ability to crystallize specific proteins with sufficient size and crystalline quality to obtain the high resolution X-ray diffraction patterns needed to solve their structure.

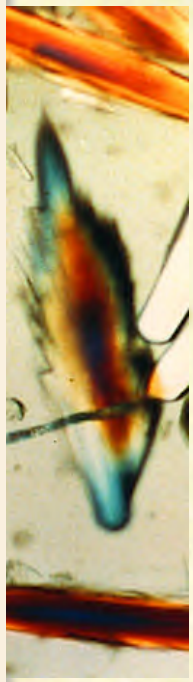
Crystals often will grow larger and with much better internal order, if made in microgravity.

X-ray diffraction data from more than 33 space-grown crystals revealed structures in much more detail than ever before, and allowed the structure of some proteins to be determined for the first time.

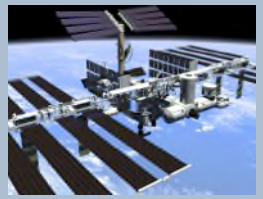
Space grown proteins ranging from insulin to HIV reverse transcriptase, demonstrated that the microgravity environment improved crystal growth over the best-case Earth-grown crystals in the following ways:

- #Larger Crystals in 45.4% of the cases
- #New Crystal Structures in 18% of the cases
- #10+% increase in the X-Ray Crystallography Brightness in 58% of the cases
- #Less thermal motion in 27.2% of the cases
- #X-Ray Crystallography resolution improved ~0.3 Angstroms in 42.4% of the cases
- #X-Ray Crystallography resolution improved 0.3 to 0.5 Angstroms in 9.9% of the cases
- #X-Ray Crystallography resolution improved 0.5 to 1.0 Angstroms in 9.9% of the cases

In the improvement of resolution, a 1 Angstrom improvement can mean the three-dimensional structure can be determined and atomic positions in the macromolecule can be resolved.

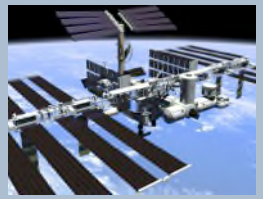


Space Biotech offers the potential of life saving advances addressing the world's top medical issues with $100B+ per year total available market potential.



Space Biotech offers the potential of life saving advances addressing the world's top medical issues with $100B+ per year total available market potential.

- **Past successes are significant and the future potential much greater** Over the past 30 years, space biosciences research has delivered life-saving and life-enhancing products that today yield more than $2B a year in product revenue (conservative estimate). Because of the biotech revolution, the promise for future dividends from space biotech research is even greater. The worldwide market for just 3 high potential areas -- infectivity, 3-D cell/tissue cultures, and plant products -- is more than $100B per year."



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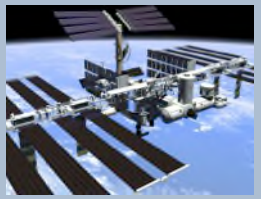
- ***Knowledge*, not in-space manufacturing, is the important ROI in early ISS research**. Once the knowledge of what factors governed gene expression and biochemical interaction is revealed in space, the results can be replicated and fine-tuned on the ground leading to new pharmaceutical products."



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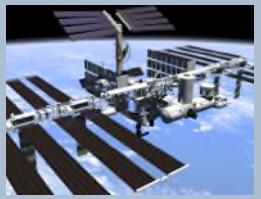
- **Microgravity causes different physical features of the growth environment to become dominant, eliciting valuable biological responses, and opportunities for unique manipulations of the environment. These features can be important for 3 dimensional cell and tissue culture and protein crystallization, relevant to cancer research, infectious disease research, development of organ bandages, and aging research. "**



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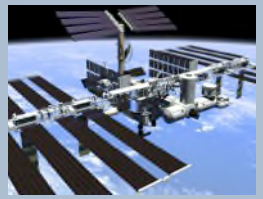
- **Rapid turnaround and high throughput are required.** Space investigations must meet current biotech throughput standards. Nominally this means launches of live specimens and research equipment at least monthly; experiments iterated within weeks; and 2-3 kilograms of samples returned to Earth approximately monthly."



2000-Present

Venture Capitalists !
Recommended Focus Areas for Space Biotech"

- #Is it worth it? "
  - # Large market size"
  - # Reasonable R&D investment"
  - # Large projected profit"
- #Is it real?"
  - # Proven science"
  - # Manufacturable product"
  - # Low government uncertainty"
- #Can we win? Is product specific"
  - # Best management team"
  - # High competitive entry barriers"

"

Venture Capitalists !
Recommended Focus Areas for Space Biotech"

- # Is it worth it? YES"
  - # Large market size? YES"
  - # Reasonable R&D investment"
  - # Large projected profit? YES"

Not Enough Yet

- # Is it real?"
  - # Proven science"
  - # Manufacturable product? YES"
  - # Low government uncertainty"

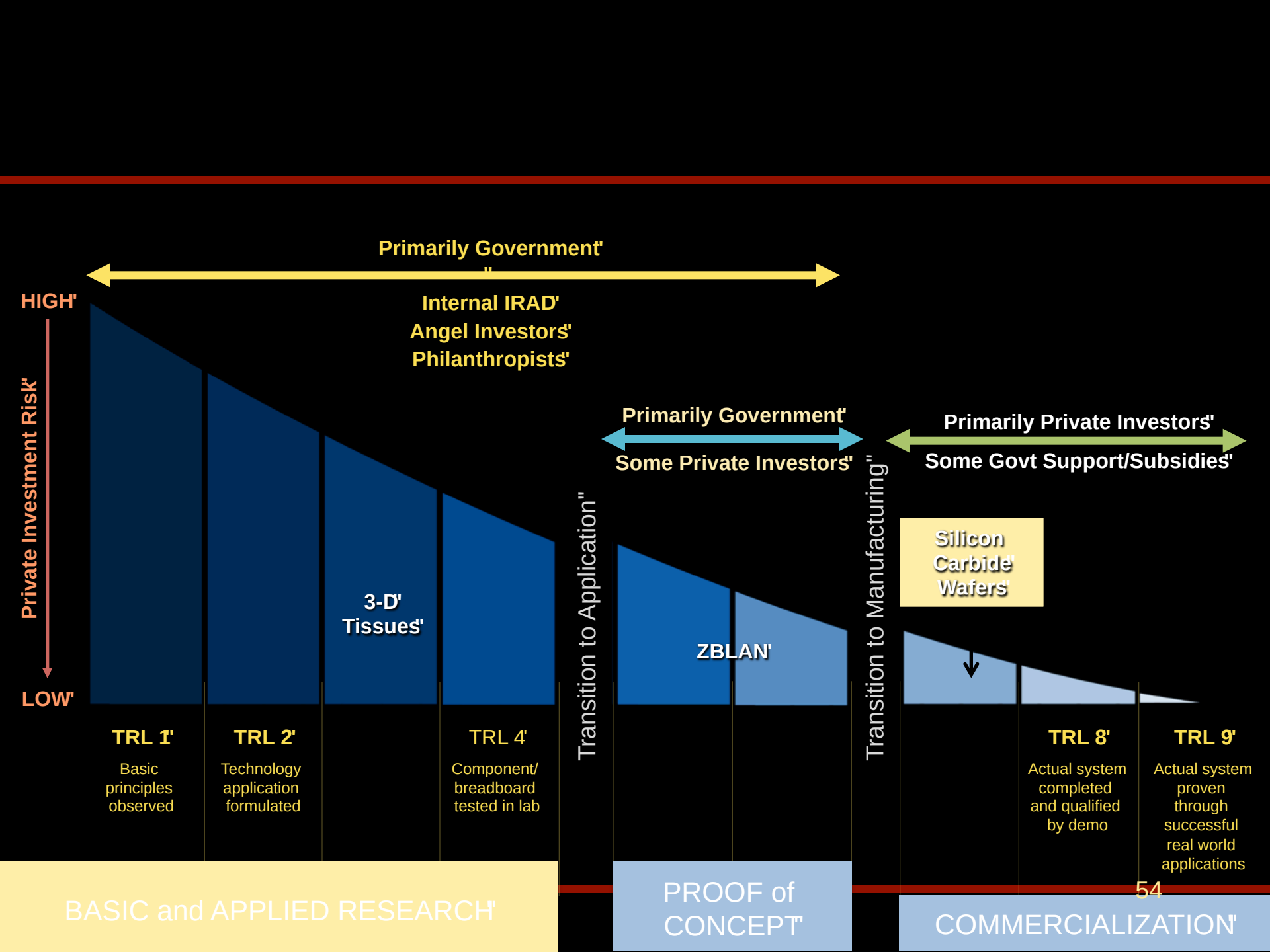
Close, needs more

No

- # Can we win? Is product specific"
  - # Best management team?"
  - # High competitive entry barriers?"

"

lynn.d.harper@nasa.gov


Primarily Government
Internal IRAD
Angel Investors
Philanthropists
HIGH
Private Investment Risk
LOW
Primarily Government
Some Private Investors
Primarily Private Investors
Some Govt Support/Subsidies
Transition to Application
Transition to Manufacturing
3-D Tissues
ZBLAN
Silicon Carbide Wafers
TRL 1
Basic principles observed
TRL 2
Technology application formulated
TRL 4
Component/ breadboard tested in lab
TRL 8
Actual system completed and qualified by demo
TRL 9
Actual system proven through successful real world applications
BASIC and APPLIED RESEARCH
PROOF of CONCEPT
COMMERCIALIZATION


2011

Approach"

- #Conduct research to demonstrate the value proposition to commercial biotech. (What needs to be demonstrated – Question for this group)"
- #Demonstrate that the logistics train works and delivers samples of sufficient quality to warrant the cost frequently enough to enable iteration and rapid learning."
- #The payload costs must be reasonable."
- #Message to NASA - Commercial biotech companies are not going to pay for suppliers to demonstrate the value proposition to them … or … that the logistics chain works."
- #NASA/government will need to prime the pump."


2016

Summary"

- # By removing gravity, growing 3-D cell and tissue cultures in space has the potential to yield much higher larger and much higher quality cultures than can currently be achieved on Earth for certain cultures. This was most recently demonstrated by Dr. Cheryl Nickerson et al for salmonella infectivity and human lung tissue (2010)."

- # Tissue cultures already grown in space show important properties and some superior features to terrestrial cultures even on the first investigations, but no one has put together a concerted effort to standardize and optimize tissue cultures in space."

- # The kind of iteration needed for space laboratory sciences, including optimizing space-grown tissue cultures for medical research, is only now becoming possible because of entrepreneurial space companies and ISS."

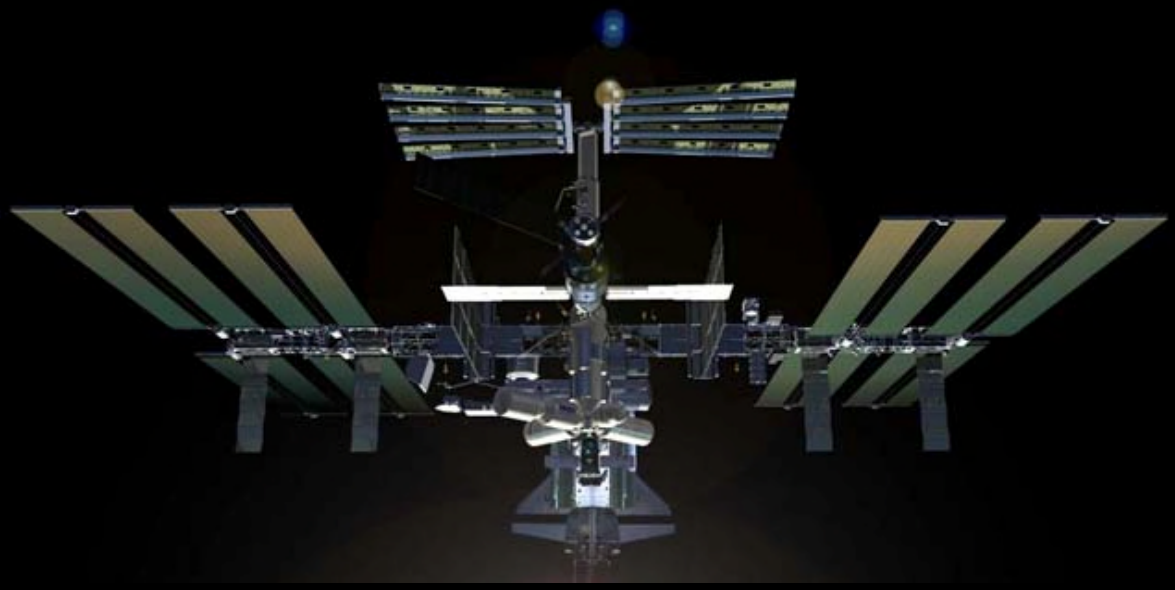
- # **The next step might be to identify cell and tissue culture targets of interest, establish performance criteria, and fly them as soon as feasible in existing systems to analyze where improvements need to be made."**

Nobel Laureate Baruch S. Blumberg and Human Genome Project Pioneer J. Craig Venter speaking at the ISS National Laboratory Workshop

“The ISS has many aspects of a field station in addition to its role as a laboratory.

It is in a remote location – in fact very remote.”

"



“But, the opportunities for new observations compensate for the difficulties.”

Nobel Laureate Baruch Blumberg
ISS National Laboratory Workshop

Baruch Blumberg's Last Words

"The project should focus at each of its phases on achieving the goal,

but also on expecting the unexpected and

assigning resources to pursue unexpected findings to new scientific, applied, and commercial outcomes."

Heraclitus (c.535 BC - 475 BC): "If you do not expect the unexpected, you will not find it; for it is hard to be sought out, and difficult".

Baruch Blumberg's Last Words"

Citizen Science can be an important feature of the project.

This can generate new ideas as there are many more participants,

and amateurs often see things professionals do not.

"Inexperience of the volunteers proved to be advantageous in that it shielded data collection against preconceived biases. The professionals often had narrow views on what they were looking for during the dig, while the volunteers were more open to finding a variety of things"
(Barreto, Fastovsky, and Sheehan (2003)

This is the biological story of the only life in the Universe that we know in our first generations beyond the planet of origin.

Space is evolutionarily novel with 5+ orders of magnitude changes in one of the fundamental organizing forces of nature: gravity.

Very different futures are available to a species that can thrive beyond their planet of origin, versus those whose destinies are constrained to a single world.